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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,590	06/01/2006	Arnold I Caplan	CWR-7781PCT/US	1634

68705 7590 10/28/2008

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
10/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,590	CAPLAN ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *3, 16-18, 20-25, 32-38, 46, 57-59, 61-67, 73-79, 84, 86-89, 97, 99, 101, 103-105, 107, 109, 110, 112, 114-119, 121-127, 130, 133-140, 142, 143, 145, 147-149, 151, 153, 154, 156, 158-163, 165-171, 177-184, 186, 188, and 189* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6,8,9,11,13-15,26,29,39,41,45,47,48,50,52,54-56,67,70,80,82,85,190 and 191* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09/22/2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-4,6,8,9,11,13-18,20-26,29,32-39,41,45-48,50,52,54-59,61-67,70,73-80,82,84-89,96, 97, 99, 101, 103-105, 107, 109, 110,112, 114-119, 121-127, 130, 133-140, 142, 143, 145, 147-149, 151, 153, 154, 156, 158-163, 165-171, 177-184,186, and 188-191.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of the invention of Group I, drawn to a cell delivery composition, in the reply filed on 07/14/2008 is acknowledged. In the same reply, Applicant elected without traverse the species of delivery via injection into the target tissue and cartilage as a target tissue.

It is noted that, in the restriction requirement mailed on 05/15/2008, Applicant was required to elect a single species from each group of progenitor cells, markers, and bioactive factors. However, Applicant elected several of the species of progenitor cells recited in claims 2 and 45, several species of the markers recited in claims 11 and 52, and several species of bioactive factors recited in claims 41 and 82. Although such a response would be normally considered non-responsive, the Examiner acknowledges that examination can proceed expeditiously without election of a specific progenitor cell, a specific marker, or a specific bioactive factor. Additionally, since the art search rendered results relevant for target tissues other than cartilage, the species election requirement between the different target tissues is hereby withdrawn.

Claims 5, 7, 10, 12, 19, 27, 28, 30, 31, 40, 42-44, 49, 51, 53, 60, 68, 69, 71, 72, 81, 83, 90-95, 98, 100, 102, 106, 111, 113, 120, 128, 129, 131, 132, 141, 144, 146, 150, 152, 155, 157, 164, 172, 173, 175, 176, 185, and 187 have been cancelled.

Claims 3, 16-18, 20-25, 32-38, 46, 57-59, 61-67, 73-79, 84, 86-89, 97, 99, 101, 103-105, 107, 109, 110, 112, 114-119, 121-127, 130, 133-140, 142, 143, 145, 147-149,

151, 153, 154, 156, 158-163, 165-171, 177-184, 186, 188, and 189 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim.

Claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191 are under examination.

Specification

2. The disclosure is objected to because of the following informalities: this application contains sequence disclosures (p. 3, lines 24-28, p. 8, lines 7-11, p. 23, lines 5, 6, and Table I) that are encompassed by the definitions for nucleotide sequences set forth in 37 CFR 1.821 (a)(1) and (d). However, the specification fails to comply with the requirements of 37 CFR 1.821 (a)(1) and (d), because the sequence identifiers, preceded by SEQ ID NO are missing.

Appropriate correction is required.

3. The use of the trademarks SASRIN and PLURONICS, and Vybrant has been noted in this application (p. 21, line 22, p. 38, line 1, p. 41, lines 8 and 10). It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Omum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, -9, 12, 14-16, 38-40, and 42 of copending Application No. 10/461,887, in view of both Simmons et al. (Progr. Clin. Biol. Res., 1994, 389: 271-280) and Gerstenfeld et al. (J. Bone Miner. Res., February 2002, 17: 221-230, Abstract). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are obvious variants.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant claims are drawn to a composition and a method of delivering a comprising a progenitor cell such as mesenchymal stem cell (MSC) (i.e., a chondrogenic cell) and a targeting moiety such as an antibody to collagen II, wherein the targeting moiety is capable of targeting the cells to a specific tissue such as cartilage, wherein the targeting moiety modified is palmitoylated or myristoylated and directly linked to the MSC or wherein the targeting moiety is linked to the MSC via a palmitoylated inker such as palmitoylated or myristoylated protein G; MSCs express markers such as Stro-1 (claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 45, 47, 48, 50, 52, 54-5667, 70, 80, 190, and 191). The composition further comprises a bioactive factor (claims 41 and 82).

The application claims are drawn to a composition comprising a chondrogenic cell and a targeting moiety linked to the chondrogenic cell, wherein the targeting moiety is an antibody to collagen II directly linked to the cell (claims 1, 4-6, 12, 14, 38-40, and 42); the antibody is palmitoylated or myristoylated (claims 7-9). The targeting antibody could be indirectly linked to the cell via protein G (claims 15 and 16). The specification defines that the chondrogenic cell could be a MSC, (p. 7, lines 7 and 8, p. 9, lines 20-30) (i.e., a cell expressing Stro-1, see Simmons et al., p. 273). The specification also discloses that the composition is used in a method of delivering the chondrogenic cells to a site of cartilage defect via injecting the composition into the cartilage (p. 3, lines 10-16, p. 19, lines 9-11). The application claims do not recite further including a bioactive

factor, such as bone morphogenic protein (BMP). Gerstenfeld et al. teach that BMP-7 induces chondrogenic differentiation of MSCs (Abstract). It would have been obvious to one of skill in the art to modify the composition recited in the application claims by further including BMP-7 to achieve the predictable result of inducing the chondrogenic differentiation of MSCs necessary to repair the damaged cartilage.

Thus, one of skill in the art would consider the instantly pending claims an obvious variation of the application claims.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 47 recites the limitation "the linker" in claim 190. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section

351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1, 2, 11, and 13-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Phillips (U.S. Patent No. 7,282,222), as evidenced by Simmons et al. (Progr. Clin. Biol. Res., 1994, 389: 271-280).

The instant claims are drawn to a composition comprising a progenitor cell and a targeting moiety, wherein the targeting moiety directs the progenitor cell to a target tissue. Such language encompasses the embodiment of a targeting moiety linked to the cell and the embodiment of a targeting moiety not linked to the cell, wherein the targeting moiety is capable of directing the cell to the desired tissue regardless of whether it is linked to the cell or not. In making the instant rejection, the claims are interpreted as reciting a targeting moiety not linked to the progenitor cell, wherein the targeting moiety directs the progenitor cell to a specific tissue.

Phillips teaches a cell delivery composition comprising mesenchymal stem cells (MSCs) and an asialoorosomucoid, wherein the asialoorosomucoid binds the asialoglycoprotein receptor in liver (i.e., a targeting moiety which binds to a target tissue, wherein the targeting moiety interacts with a protein epitope intrinsic to the target tissue) and wherein the binding of asialoorosomucoid to the asialoglycoprotein receptor selectively directs the MSCs to the liver (i.e., selectively directs the progenitor cells to the target tissue) (claims 1, 2, and 13-15) (column 6, lines 5-15). With respect to the markers recited in claim 11, it is noted that expressing Stro-1 is an inherent property of MSCs (see Simmons et al., p. 273). Since Phillips teaches al claim limitations, the claimed invention is anticipated by the above-cited art.

10. Claims 1, 2, 8, 11, 13-15, 29, 39, 45, 52, 54-56, 70, 80, and 190 are rejected under 35 U.S.C. 102(e) as being anticipated by Lum et al. (PGPUB 2006/0034767).

Lum et al. teach a method of delivering a stem cell to a target tissue by administering a composition comprising a stem cell and a bispecific monoclonal or polyclonal antibody linked to the stem cell, wherein the bispecific antibody has a first antigen binding site which binds to the stem cell and a second antigen binding site which binds a specific antigen on a target tissue, and wherein the stem cell is specifically delivered to the target tissue bearing the antigen recognized by the bispecific antibody (claims 1, 8, 13-15, 29, 54-56, 70, and 190) (Abstract, p. 1, paragraphs 0002 and 0011-0017, p. 2, paragraphs 0018 and 0019). Lum et al. teach that the stem cell could be a hematopoietic stem cell expressing CD34, wherein the hematopoietic stem cell could be targeted to the heart (claims 2, 11, 39, 45, 52, and 80) (p. 2, paragraphs 0022-0024, p.3, paragraphs 0050 and 0062, p. 5, paragraph 0072). Since Lum et al. teach all the claim limitations, the claimed invention is anticipated by the above-cited art.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1, 2, 4, 6, 8, 9, 11, 13-15, 26, 29, 39, 41, 45, 47, 48, 50, 52, 54-56, 67, 70, 80, 82, 85, 190, and 191 are rejected under 35 U.S.C. 103(a) as being unpatentable over Logtenberg et al. (WO 00/23570), in view of each Colsky et al. (J. Immunol. Methods, 1989, 124: 179-187), Kim et al. (J. Immunol. Methods, 1993, 158: 57-65), Caplan et al. (Trends in Molecular Medicine, 2001, 7: 259-264), Thomas et al. (Annals of the Rheumatic Diseases, 1994, 53: 488-496), and Simmons et al (Progr. Clin. Biol. Res., 1994, 389: 271-280).

Logtenberg et al. a method of tissue repair by delivering a cell to a target tissue in a subject, wherein delivery takes place via administration of a composition comprising the cell coated with a targeting moiety, wherein the targeting moiety could be a lipid-modified antibody, and wherein the binding of the targeting moiety to the target tissue selectively directs the cell to the target tissue; Logtenberg et al. also teach that the cells could be genetically modified such as to express IL-2, i.e., the composition comprises a bioactive factors such as an interleukin (claims 1, 8, 13-15, 29, 41, 54-56, 70, 82, and 190) (Abstract, p. 2, lines 24-27, p. 3, lines 23-33, p. 4, lines 1-11 and 29-31, p. 6, lines 1-15, p. 9, lines 4-28, p. 14, lines 8-14, p. 15, lines 19-30).

Although Logtenberg et al. teach coating their cells with lipid-modified antibodies, they do not specifically teach palmitoylated antibodies or attaching the antibody via a palmitoylated protein A linker (claims 4, 6, 9, 47, 48, 50, and 191). However, at the time the invention was made, the use of palmitoylated antibodies or of palmitoylated protein A to coat cells with antibodies was taught by the prior art. For example, Colsky et al. teach coating cells with palmitoylated antibodies (Abstract, p. 180, column 1) and Kim et

al. teach coating cells with antibodies by using a palmitoylated protein A linker (Abstract, p. 57, column 2, p. 58, column 1, first paragraph). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the composition of Logtenberg et al. by using palmitoylated antibodies or a palmitoylated protein A linker to achieve the predictable result of coating the cells with antibodies.

Although Logtenberg et al., Colsky et al., and Kim et al. teach tissue repair, they do not specifically teach injecting the cell directly into the tissue, wherein the tissue could be cartilage or bone, nor do they teach the cell as being a MSC (claims 2, 39, 45, 80, 85). Caplan et al. teach using MSCs for the tissue repair and the need to specifically target the MSCs to the desired tissue for increased therapeutic efficiency; Caplan et al. also teach that the tissue could be bone or cartilage and that the MSCs could be genetically modified to express bone morphogenic proteins and could be directly injected into the cartilage (p. 261, column 1, p. 262, column 1). Based on these teachings, it would have been obvious to one of skill in the art, at the time the invention was made, to use the method of Logtenberg et al., Colsky et al., and Kim et al. with MSCs to achieve the predictable result of specifically targeting the cells to the damaged cartilage or bone with the purpose of regenerating the damaged cartilage or bone.

Although Logtenberg et al., Colsky et al., Kim et al., and Caplan et al. teach specific delivery to cartilage by using antibody-coated MSCs, they do not specifically teach using anti-collagen II antibodies (claims 26 and 67). However, it is noted that the prior art teaches that collagen II is a cartilage-specific collagen (see Thomas et al., p. 488, column 1). Therefore, it would have been obvious to one of skill in the art, at the

time the invention was made, to use an anti-collagen II antibody in the method of Logtenberg et al., Colsky et al., Kim et al., and Caplan et al. to achieve the predictable result of targeting their MSCs to the cartilage tissue.

With respect to the limitation of Stro-1 as a marker (claims 11 and 52), it is noted that the art teaches that MSCs express Stro-1 (see Simmons et al., p. 273).

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

13. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner, Art Unit 1633